PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P.ULB.91/WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/BE 03/00131	International filing date (day/month/year) 04.08.2003	Priority date (day/month/year) 02.08.2002
International Patent Classification (IPC) or both national classification and IPC A61K38/17		
Applicant UNIVERSITE LIBRE DE BRUXELLES et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14.02.2004	21.10.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Pilling, S Telephone No. +49 89 2399-8461

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/BE 03/00131

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-29 as originally filed

Sequence listings part of the description, Pages

1-5 as originally filed

Claims, Numbers

1-18 as originally filed

Drawings, Sheets

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-10,14-16 .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10,14-16
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-10,14-16
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-10,14-16
	No:	Claims	

2. Citations and explanations

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/BE 03/00131

see separate sheet

Re Item IV

Lack of unity of invention

1. In agreement with the findings of the International Searching Authority (See the comment accompanying the INVITATION TO PAY ADDITIONAL FEES), it is considered that there is lack of unity of invention (Rule 13.1 PCT) in respect of the present claims. In this regard, there is no technical relationship involving one or more of the same or corresponding special technical features (Rule 13.2 PCT) between the subject-matter of the following groups of claims:

   a) Claims 1 to 10; pharmaceutical compositions/uses comprising apolipoprotein L-I (apoL-I), an active fragment thereof, a polynucleotide encoding apoL-I, a cell transformed with the latter polynucleotide or an apoL-I inhibitor

   b) Claims 11 to 13; diagnostic kits comprising apoL-I, a fragment thereof, a polynucleotide encoding apoL-I or an apoL-I inhibitor

   c) Claims 14 to 16; non-human genetically modified mammals which express a polynucleotide encoding apoL-I or a fragment thereof and are resistant to Trypanosomal diseases

   d) Claims 17 or 18; solid supports/methods for recovering apoL-I from a mammal using an immobilised apoL-I inhibitor

2. The following examination has been carried out in respect of inventions (a) and (c) as identified above for which International Search and Preliminary Examination fees have been paid.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

3. The documents cited in the International Search Report (ISR) are consecutively numbered D1 to D7 in the order of their listing. If not indicated otherwise, reference is made to the passages cited in said ISR.

invention (a)

4. None of the presently available prior documents discloses pharmaceutical compositions comprising apolipoprotein L-I (apoL-I), an active fragment thereof, a polynucleotide encoding apoL-I, a cell transformed with the latter polynucleotide or an apoL-I inhibitor. Thus, the subject matter of Claims 1 to 10 is new (Article 33(2) PCT).

5. The closest prior art in respect of Claims 1 to 10 appears to be document D1 since this document discloses that apoL-I is a trypanolytic factor (TLF) in human blood (see the abstract). Document D1 further indicates "*The potential of exploiting a natural non-immune killing factor, TLF as an alternative chemotherapy for African trypanosomiasis deserves further investigations*" (see the final paragraph of the Discussion). Thus, it appears *prima facie* that document D1 suggests the administration of a medicament based on apoL-I.

6. The Applicant has however argued that the teaching of document D1 is in fact erroneous since the molecule identified in document D1 as apoL-I is not apoL-I but is a different molecule. The Applicant has pointed to the discrepancy between the apparent molecular weight of apoL-I as derivable from Figure 2c in D1 (greater than 80 kDa) and the molecular weight of apoL-I indicated in document D3 (42kDa) as support for this view. Thus, in the absence of any contrary evidence showing that the molecule described in document D1 was apoL-I, the International Examining Authority have accepted the arguments of the Applicant. Thus, it appears that the erroneous teaching of document cannot for the basis for a finding of lack of inventive step in respect of the subject matter of present Claims 1 to 10.

7. None of the further pre-published documents disclose that apoL-I is a trypanolytic factor.

8. Thus, the subject matter of Claim 1 to 10 appears to be inventive (Article 33(3) PCT).

invention (c)

9. None of the presently available prior art documents disclose a genetically modified mammal expressing an apoL-I polynucleotide/polypeptide. Thus, the subject matter of Claims 14 to 16 is new.

10. None of the presently available prior art documents suggest or teach towards the production of a genetically modified mammal expressing an apoL-I polynucleotide/polypeptide. In this regard, documents D6 and D7 each disclose genetically modified mammals expressing different apolipoproteins (A, B or E) for investigating neuronal/atherosclerotic diseases. There is no suggestion in these documents, however, of expression of apoL-I. Moreover, in the absence of any further disclosure in the prior art relating to apoL-I as a trypanolytic factor, it must be concluded that there was no motivation for the skilled man to produce genetically modified mammals expressing an apoL-I polynucleotide/polypeptide. The present Applicant's disclosure that such mammals can be used as models for studying Trypanosomal diseases does not appear to have been predictable on the basis of the prior art. Thus the subject matter of Claims 14 to 16 appears to be inventive.